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EXAMINER

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Paper No. 58

Application Number: 08/238,405

Filing Date: May 5, 1994

Appellant(s): Capon et al.

Dean H. Nakamura

For Appellant

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EXAMINER'S ANSWER

This is in response to the appeal brief filed December 13, 2002.

(1) Real Party in Interest

A statement identifying the real party in interest is contained in the brief.

(2) Related Appeals and Interferences

A statement identifying the related appeals and interferences which will directly affect or be directly affected by or have a bearing on the decision in the pending appeal is contained in the brief. However, the meaning of the second paragraph on page 16 of the Brief is unclear (i.e., as it relates to whether Appellant is aware of issued patents that may interfere with that claimed in the instant application).

(3) Status of Claims

The statement of the status of the claims contained in the brief is correct.

(4) Status of Amendments After Final

The appellant's statement of the status of amendments after final rejection contained in the brief is correct.

(5) Summary of Invention

The summary of invention contained in the brief is correct.

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(6) Issues

The appellant's statement of the issues in the brief is correct.

(7) Grouping of Claims

Claims 57, 64, 65, 67 and 69 stand or fall together, as stated by appellant.

(8) ClaimsAppealed

The copy of the appealed claims contained in the Appendix to the brief is correct.

(9) Prior Art of Record

The following is a listing of the prior art of record relied upon in the rejection of claims under appeal.

5,906,936

Eshhar et al.

5-1999

(10) Grounds of Rejection

The following ground(s) of rejection are applicable to the appealed claims:

A) Claims 57, 64-65, 67 & 69 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

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No proper antecedent basis nor conception in context with that described within the specification at the time of filing the instant application exists for the broader and generic negative recitation of "in the absence of a T-cell receptor". In contrast, the proper context described in the paragraph bridging pages 30 & 31 of the specification is that a "CD8/ ζ " chain can be used as the cytoplasmic signaling domain in a Jurkat T cell leukemic line, JRT3.T3.5, which contains a mutated and non-functional T-cell receptor, and therefore, results "in the absence of TCR [T-cell receptor] *expression on the cell surface* [emphasis added]". In other words, a mutated T-cell receptor still exists in these cells, which does not become functional, and presumably is not expressed on the cell surface, until the ζ (zeta) chain is added. Therefore, the generic recitation of excluding any T-cell receptors (i.e., including mutated T-cell receptors) from cells that must be used to construct the chimeric protein of the instant invention was not reasonably contemplated at the time of filing Appellants' invention; thereby, constituting new matter.

Note that if claim 57 recited "in the absence of a wildtype T-cell receptor expressed on the cell surface... wherein said cytoplasmic domain consists of a zeta chain, and when said protein is then expressed as a membrane bound protein...", this rejection would have been obviated. Moreover, claim 57 would then no longer recite different cytoplasmic domains (i.e., as recited in the Markush group of claim 57) not contemplated to be used in cells containing a mutated T-cell receptor.

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B) Claims 57, 64, 67 & 69 stand rejected under 35 U.S.C. 102(e) as being anticipated by Eshhar et al. (U.S. Patent 5,906,936).

Eshhar et al. teach creation of a membrane bound chimeric antibody (Ab)/ T-cell receptor (TcR) chimeric protein (i.e., still containing the T-cell receptor-derived tyrosine kinase activity; as it relates to claim 57), in which the extracellular TcR V[variable] domain (i.e, α and β chains) are replaced with either the extracellular “variable... heavy (H) or light (L) chain” of a “antibody for a predefined antigen” (i.e., a single chain antibody variable (V) domain; column 4 (lines 18-29 & 6-9); columns 5-7; Figure 4; as it relates to claim 57). In other words, Eshhar’s chimeric protein is created to express on the surface of a cell and “comprises” in the N-terminal to C-terminal region an “extracellular antigen-binding domain” region naturally joined to the “transmembrane domain” of the “TcR/CD3” receptor (column 3, line 66), and then to a TcR/CD3 “cytoplasmic domain” comprising the constant region of the T-cell receptor, γ and/or δ chains (e.g., column 4, lines 6-7; column 6 & Figures 8-9), which thereby “initiates/transduces a signal resulting in activation of a secondary messenger system (i.e., as evidenced by IL-2 production in the MTT assay; Table I, Figures 1 & 4; column 2; and where “stimulation through the cTcR triggered the T cell hybridoma to its full activity”; column 10, lines 9-11; as it relates to claim 57). In that Eshhar also teach making their chimeric protein construct in mutated human/mammalian Jurkat cells, such as in column 9 (line 64), which describes use of “a TcR [T-cell receptor] deficient mutant (27J)”, and Table I, which demonstrates use of the cytotoxic T lymphocyte “(CTL) hybridoma lacking the TcR chain”, where neither of these cell lines would be recognized as foreign in an appropriate host due to them being “not-restricted by self-MHC

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molecules" (e.g., see column 10, line 52-54; column 2, lines 26-31; as it relates to claim 69), the limitation of "in the absence of a T-cell receptor" (i.e., as it relates to claims 57) and claims 64, 67 & 69 are anticipated.

(11) Response to Argument

Issue A: Appellants argue on pages 14-16 of the brief that "the invention may have been misunderstood", that "[t]o satisfy the written description requirement, a disclosure does not have to prove in haec verba support for the claimed subject matter so long as one of ordinary skill can recognize that the applicant invented what was claimed", cites *In re Anderson, Purdue Pharma L.P v. Faulding Inc.*, *In re Aston, Jacobs v. Lawson, Ex parte Davisson et al.* and *In re Slocombe*, and then makes new reference to "Letourneau & Klausner", "Eshhar et al.", "Kolanus et al", and "[unknown] recently issued patents". However, because Appellants fail to give proper citations for these references, it can only be assumed by the Examiner that they refer to IDS reference #s AO, AK and AN (filed 5/19/96; Paper No:16), respectively, which have publication dates 2 years, 3 years and 3 years, respectively, after the claimed priority date of the instant application (i.e, 1990). Nevertheless, it is confusing whether Appellants' are attempting to argue that others invented the instant invention, or argue that their invention is enabled. In either case, these references are irrelevant to the pending rejection of new matter under 35 U.S.C., first paragraph, and appear to merely confuse the record. However, it is acknowledged Appellants are correct that the zeta chain is of the T-cell receptor (Tc receptor) and not of the Fc receptor, which is obviously a typographical error that does not change the rejection of record.

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In contrast to Appellants' assertions on pages 14-16 of the brief, the issue is simply that pages 30-31 of the specification solely appear to contemplate transfection of the ζ (zeta) chain of the "Tc receptor [CD3]" in a mutated T-cell Jurkat cell line, where the issue then becomes whether the generic negative limitation of "in the absence of a T cell receptor" is properly contemplated in order to overcome the previously cited 102(b) art (e.g., see Paper No: 41; mailed 10/04/00). In other words, it is not reasonable to extrapolate from the limited disclosure of using a cell line where a mutated and nonfunctional T-cell receptor is expressed (and where the claims alternatively do not recite "in the absence of a mutated T-cell receptor") to the generic concept of "in the absence of a T cell receptor". Second, if it is found by the court that the recitation of "in the absence of a T-cell receptor" is not new matter, mixing and matching different non-zeta chain cytoplasmic domains with a mutated T-cell receptor, in order to create a "chimeric protein" receptor would then reasonably constitute new matter.

Thus, in contrast to Appellants' assertions, the issue has nothing to do with "[t]he Examiner has provided no evidence to even suggest that any particular members of molecules that can comprise a cytoplasmic domain would not operate as alleged in the instant application", nor whether "the instant application clearly conveys to the artisan that the chimeric receptors of interest can operate independent of a T cell receptor as a signaling molecules", because the issue again is new matter, and not "inherency", nor enablement under 35 U.S.C. 112, first paragraph.

In conclusion, because the disclosure of adding solely the ζ (zeta) chain of the Tc receptor/CD3 to a mutated T-cell receptor is not the same concept as generically adding a "cytoplasmic domain which initiates a signal.... selected from... CD3 eta chain, CD3 gamma

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chain, CD3 delta chain, CD3 epsilon chain, the gamma chain of the Fc receptor and tyrosine kinase” “in the absence of a T cell receptor”, as recited in claim 57, and because the claims are broader in concept than “transduces a signal... in the absence of a [functional] T-cell receptor [expressed on the cell’s surface]”, the current claims should reasonably constitute new matter.

Issue B: Appellants argue on pages 17-19 of the brief that Gross et al., “Goverman et al. and Weiss were provided to demonstrate the state of the art in a reply to an Office Action”, and then cite MPEP 609C(3). However, MPEP 609 C(3) states that a reference not made part of an IDS is considered to “the extent that a document is submitted as evidence directed toward an issue of patentability raised in an Office Action...”, in which neither Paper No: 29 (page 6) nor Paper No: 43 (page 7) nor Weiss state that “the gamma and delta chains of Eshhar et al. are not the same as the CD3 gamma and CD3 delta chains of the instant invention”, nor that “[t]he art was well aware of that distinction as noted by Weiss”. Moreover, nowhere is any structure recited in the claims (e.g., SEQ ID NO) that distinguishes use of Eshhar’s gamma (γ) and delta (δ) chains from that of the instant invention, which alternatively appear to be identical to that recited in the claims. In other words, Appellants’ supposition that “[t]he gamma and delta chains of Eshhar et al. are not the same as the CD3 gamma and CD3 delta chains of the instant invention” has no definitive support, and simply is incorrect; especially when taken into account that Eshhar’s gamma (γ) and delta (δ) chains are derived from the same T-cell receptor (TcR)/CD3 as that claimed (e.g., see column 3, last paragraph; column 9, lines 3-6). Thus, Appellants’ arguments are not on point and mischaracterize that disclosed by both Weiss and Goverman et al.

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Appellants then argue that "it is clear that because Eshhar et al. is essentially shuffling variable and constant domains between immunoglobulin and immunoglobulin-like molecules such as alpha, beta, gamma and delta chains of Ti, Eshhar et al. clearly is distinct from the instant invention". In contrast to Appellants' assertions, Eshhar et al. specifically disclose that "according to the present invention, there were constructed chimeric T cell receptor genes by recombining the V_H and V_L gene segments of an anti-TNP antibody with the constant region exons of the T cell receptor's (TcR) α and β chain" (column 3, lines 42-46), which clearly meets the limitations for "a chimeric protein *comprising* in the N-terminal to C-terminal region an extracellular antigen-binding domain of a single chain antibody that binds specifically to an antigen [emphasis added]" (e.g., TNP). Second, consistent with Appellants' discussion on pages 10-13 of the brief, Eshhar et al. teach that "[a]lthough ligand binding to the T cell receptor initiates two early activation signals (calcium raised and PKC activation) as reviewed in Weiss et al...., they are not sufficient to cause IL-2 production and proliferation of T cells...". Thus, because Eshhar's chimeric protein "initiates/ transduces a signal resulting in activation of a secondary messenger system (i.e., as evidenced by IL-2 production in the MTT assay; Table I, Figures 1 & 4; column 2), Eshhar et al. obviously teach the same CD3 gamma and delta chains as in the instant invention, because otherwise, no signal for Il-2 secretion would be transduced/ initiated; consistent with that stated by Weiss.

Lastly, Appellants argue on page 19 of the brief that Eshhar's host cells "express T cell receptor". In contrast to this assertion, Eshhar et al. also teach making their chimeric protein construct in mutated human/mammalian Jurkat cells (e.g., column 9, line 64), using "a TcR [T-

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cell receptor] deficient mutant (27J)", and/or the cytotoxic T lymphocyte (CTL) hybridoma, lacking the TcR chain (Table I). Therefore, Appellants' arguments that Eshhar's host cells all "express T cell receptor" are simply misleading and not on point. However, it should be noted that the reason Gross et al was removed as 102(b) prior art was because they did not specifically disclose use of a "TcR deficient mutant", unlike Eshhar et al. ('936).

In conclusion, Eshhar ('936) teach the same as recited in claim 57 for a "chimeric protein comprising... an extracellular antigen-binding domain of a single chain antibody that binds specifically to an antigen... a transmembrane domain... a cytoplasmic domain which initiates a signal resulting in activation of a secondary messenger system in the absence of a T-cell receptor, wherein said cytoplasmic domain is selected for... the CD3 gamma chain, the CD3 delta chain... and tyrosine kinase", as claimed. Therefore, because no where in the current claims nor instant specification is there any recitation nor description of any structure (e.g., SEQ ID NO) that distinguishes the instant invention from Eshhar's chimeric protein, because of the arguments presented above by the Examiner, and because Appellants' arguments center on α and β subunits and sections of Eschar et al. not relied upon for the instant rejection (e.g., as argued on pages 18-19 of the brief), there is no distinction between Eshhar's chimeric receptor protein, and that claimed.

Accordingly, it is noted that the courts have held that:

"the PTO can require an applicant to prove that the prior art products do not necessarily or inherently possess the characteristics of his claimed product. Accordingly, since the issue in the present appeal is whether the prior art factor is identified or patently indistinct from that of the material on appeal, appellants have the burden of showing that inherency is not involved". *Ex parte Gray*, 10 USPQ 2d 1922 (1989); *In re Best*, 195 USPQ 430 (CCPA 1976).

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Further, the courts have held that "when the prior art discloses a product which reasonably appears to be either identical with or only slightly different than a product..., a rejection based alternatively on either section 102 or section 103 of the statute is eminently fair and acceptable".

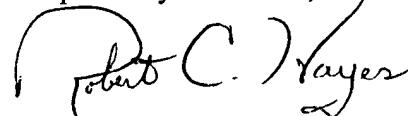
In re Brown, 173 USPQ 685 (1972).

Thus, Appellants' arguments are not on point and should not be found persuasive.

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For the above reasons, it is believed that the rejections should be sustained.

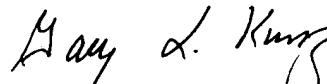
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